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Concurrent session 7: Specification and Lineage Allocation During Development

Program/Abstract # 37

Redefining brain serotonergic neurons by genetic lineage and selective *in vivo* silencing

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Central serotonin-producing neurons are heterogeneous – differing in embryonic origin, final location, morphology, firing properties, and associated clinical disorders – but the underpinnings of this heterogeneity are largely unknown, as are molecular markers capable of distinguishing among functional subtypes. To examine this heterogeneity, we have generated genetic tools for use in mice that allow multiple features of a neuron type to be delineated and linked in vivo, for example, its origin in the embryo, fate in the adult, and function in particular circuits as relates to behavior and physiology. Our starting point has been development of a dual recombinase-based molecule delivery system with plug-n-play modularity such that most any genetically-encoded lineage tracer or effector molecule can be incorporated and delivered in vivo to most neuron types. Neuron types are defined by combinatorial gene expression, making cell-type specificity high. Using these tools, we have generated a new classification scheme for serotonin neurons that is based on genetic programs differentially enacted among serotonergic precursor cells and which represents a more mechanistic view of serotonergic neuron heterogeneity than offered by anatomical segregation. Neuronal silencing tools to plot cellular functions to these different serotonergic lineages will be presented. Through these approaches, we are redefining the roles served by specific serotonin neuron subtypes in behavior and physiological homeostasis.

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Program/Abstract # 38

Lineage tracing of Tbx4-expressing cells reveals cryptic developmental decisions

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Vasculogenesis is the de novo formation of blood vessels out of undifferentiated mesenchyme, which occurs only in the regions of the embryo that produce hematopoietic stem cells: the allantois, yolk sac, and AGM regions. Mutating Tbx4, a T-box gene thought to be expressed throughout the allantois, causes defective vasculogenesis in which endothelial cells differentiate but do not coalesce into tubules. We examined Tbx4 expression at cellular resolution and traced the fate of Tbx4-expressing cell lineages using a Cre knock-in of Tbx4 with a Cre reporter line. We observe that a subset of cells in the interior of the allantois do not express Tbx4, and comparison of these cells to endothelial markers suggests that Tbx4 is expressed in a reciprocal pattern with endothelial genes. Double staining with endothelial markers and the Tbx4 lineage reporter reveals that the endothelium is entirely derived from cells that never express Tbx4, which represent a cryptic compartment within the allantois. This work is the first observation that vasculogenic mesenchyme, presumed to be naïve, is actually prepatterned. This work also shows that the vascular phenotype of the Tbx4 knockout is due to defects in perivascular tissue, as the endothelium does not express Tbx4. Tbx4 expression has also been reported in the hindlimb and external genitalia. We have examined this expression and Tbx4 lineage and we observe that, rather than separate domains, the allantois, hindlimb, and genital tubercle all arise from a single contiguous mesenchymal Tbx4- positive domain. We also note that while Tbx4 has been described as hindlimb-specific, we observe two domains of Tbx4 expression in the forelimb that contribute to distinct structures.

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Program/Abstract # 39

Genetic and genomic dissection of a cell specification pathway in *Arabidopsis*

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The Arabidopsis root epidermis provides a simple model for studying the fundamental problem of cell fate specification. Root-hair cells are specified in the space between underlying cortical cells (the H cell position) and non-hair cells are specified over a single cortical cell (the N cell position). This simple relationship between cell position and cell type differentiation implies that cell-cell communication events are important in the establishment of cell fates. Cellular, molecular, genetic, and genomic approaches have been used to define and analyze genes and their corresponding proteins that are used for the specification of the hair and non-hair cell types. Some of these genes (e.g. GLABRA2 (GL2), TRANSPARENT TESTA GLABRA (TTG), WEREWOLF (WER), GLABRA3 (GL3), and ENHANCER OF GLABRA3 (EGL3)) encode transcription factors important for non-hair cell specification, whereas others (e.g. CAPRICE (CPC), TRIPTYCHON (TRY), and ENHANCER OF TRY AND CPC (ETC1)) help to specify the hair cell type. By studying the expression and interactions